

WHAT IS CLAIMED IS:

1. A method of correlating gene and protein expression in a biological sample, the method comprising the steps of:

- a) obtaining the biological sample ;
  - b) generating a gene expression profile of the sample, thereby identifying an mRNA expressed in the sample;
  - c) identifying a physio-chemical property of a polypeptide encoded by the mRNA;
  - d) fractionating polypeptides in the sample on the basis of the physio-chemical property and;
  - (e) identifying the polypeptide encoded by the mRNA from among the fractionated proteins, wherein the identified polypeptide comprises the physio-chemical property;
- thereby correlating gene and protein expression in the sample.

2. The method of claim 1, wherein the biological sample comprises a cell lysate from a healthy cell.

3. The method of claim 1, wherein the biological sample comprises a cell lysate from a pathological cell.

4. The method of claim 1, wherein the biological sample comprises a cell lysate from a cell contacted by a toxic compound.

5. The method of claim 1, wherein the biological sample comprises a cell lysate from a cell of a subject who respond to a drug treatment or a subject who does not respond to a drug treatment.

6. The method of claim 1, wherein the biological sample comprises a cell lysate from a cell exposed to heat, cold, or radiation.

7. The method of claim 1, wherein the biological sample comprises a human cell.

8. The method of claim 1, wherein the step of generating the gene expression profile comprises identifying expressed mRNA with an EST array.

1                   9.       The method of claim 1, wherein the step of generating the gene  
2 expression profile comprises identifying expressed mRNA with an oligonucleotide array.

1                   10.     The method of claim 1, wherein the step of generating the gene  
2 expression profile comprises identifying expressed mRNA with an mRNA array.

1                   11.     The method of claim 1, wherein the mRNA is differentially  
2 expressed in two biological samples.

1                   12.     The method of claim 11, wherein the two biological samples are  
2 derived from a normal cell and a pathologic cell.

1                   13.     The method of claim 12, wherein the pathologic cell is a cancer  
2 cell.

1                   14.     The method of claim 11, wherein the two biological samples are  
2 derived from a healthy cell and a cell exposed to a toxic compound.

1                   15.     The method of claim 1, wherein the step of identifying the physio-  
2 chemical property of the polypeptide encoded by the mRNA further comprises  
3 identifying a plurality of physio-chemical properties.

1                   16.     The method of claim 1, wherein the step of identifying a physio-  
2 chemical property comprises predicting the masses of proteolytic fragments generated by  
3 the polypeptide encoded by the mRNA upon degradation of the polypeptide by a selected  
4 proteolytic agent, and the step of identifying the polypeptide encoded by the mRNA  
5 comprises subjecting polypeptides in the sample to degradation by the agent and  
6 identifying actual proteolytic fragments in the sample having masses that correspond to  
7 the masses of the predicted fragments.

1                   17.     The method of claim 1, wherein the physio-chemical property is  
2 selected from the group consisting of: amino acid sequence, molecular weight, iso-  
3 electric point, hydrophobicity, hydrophilicity, glycosylation, phosphorylation, epitope  
4 sequence, ligand binding sequence, charge at a specified pH, and metal chelate binding.

1                   18.     The method of claim 1, wherein the step of fractionating the  
2 polypeptides in the sample comprises 2D-gel electrophoresis.

1 19. The method of claim 1, wherein the step of fractionating the  
2 polypeptides in the sample comprises mass spectrometry.

1 20. The method of claim 1, wherein the step of fractionating the  
2 polypeptides in the sample comprises surface enhanced laser desorption ionization,  
3 wherein the surface enhanced laser desorption ionization comprises fractionating by  
4 affinity retention on solid phase-bound adsorbent followed by fractionating retained  
5 polypeptides from the solid phase by gas phase ion spectrometry.

1 21. The method of claim 20, wherein the adsorbent is selected to have  
2 affinity for polypeptides possessing at least one physio-chemical property selected from  
3 the group consisting of: amino acid sequence, molecular weight, iso-electric point,  
4 hydrophobicity, hydrophilicity, glycosylation, phosphorylation, epitope sequence, ligand  
5 binding sequence, charge at a specified pH, and metal chelate binding.

1 22. The method of claim 1, wherein the step of identifying the  
2 polypeptide comprises selecting a polypeptide from among the fractionated polypeptides,  
3 which selected polypeptide comprises the physio-chemical property, identifying the  
4 selected polypeptide and correlating the identity of the selected polypeptide with the  
5 polypeptide encoded by the mRNA.

1 ~~23.~~ A method of correlating gene and protein expression in a biological  
2 sample, the method comprising the steps of:

3 a) obtaining a biological sample;

4 b) generating a gene expression profile of the sample using a nucleic acid  
5 array, thereby identifying an mRNA expressed in the sample;

6 c) identifying a physio-chemical property of a polypeptide encoded by the  
7 mRNA;

8 d) fractionating polypeptides in the sample on the basis of the physio-  
9 chemical property, using mass spectrometry and;

10 (e) identifying the polypeptide encoded by the mRNA from among the  
11 fractionated proteins, wherein the identified polypeptide comprises the physio-chemical  
12 property;

13 thereby correlating gene and protein expression in the cell.

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1                   24.    The method of claim 23; wherein the step of generating the gene  
2   expression profile comprises identifying expressed mRNA with an EST array.

1                   25.    The method of claim 23; wherein the step of generating the gene  
2   expression profile comprises identifying expressed mRNA with an oligonucleotide array.

1                   26.    The method of claim 23; wherein the step of generating the gene  
2   expression profile comprises identifying expressed mRNA with an mRNA array.

1                   27.    The method of claim 23; wherein the step of identifying the  
2   polypeptide encoded by the mRNA comprises fractionating polypeptides in the sample by  
3   surface enhanced laser desorption ionization, wherein the surface enhanced laser  
4   desorption ionization comprises fractionating by affinity retention on solid phase-bound  
5   adsorbent followed by fractionating retained polypeptides from the solid phase by gas  
6   phase ion spectrometry.

1                   28.    A method of correlating gene and protein expression in a biological  
2   sample, the method comprising the steps of:

3                   a) obtaining a biological sample;

4                   b) generating a gene expression profile of the sample using an  
5   oligonucleotide array, thereby identifying an mRNA expressed in the sample;

6                   c) identifying a physio-chemical property of a polypeptide encoded by the  
7   mRNA;

8                   d) fractionating polypeptides in the sample on the basis of the physio-  
9   chemical property with surface enhanced laser desorption ionization, wherein the surface  
10   enhanced laser desorption ionization comprises fractionating by affinity retention on solid  
11   phase-bound adsorbent followed by fractionating retained polypeptides from the solid  
12   phase by gas phase ion spectrometry; and

13                  e) identifying the polypeptide encoded by the mRNA from among the  
14   fractionated proteins, wherein the identified polypeptide comprises the physio-chemical  
15   property;

16                  thereby correlating gene and protein expression in the cell.

1                   29.    The method of claim 28, wherein the adsorbent is selected to have  
2   affinity for polypeptides possessing at least one physio-chemical property selected from

3 the group consisting of: amino acid sequence, molecular weight, iso-electric point,  
4 hydrophobicity, hydrophilicity, glycosylation, phosphorylation, epitope sequence, ligand  
5 binding sequence, charge at a specified pH, and metal chelate binding.

1 30. The method of claim 28, wherein the step of identifying the physio-  
2 chemical property comprises predicting the masses of proteolytic fragments generated by  
3 the polypeptide encoded by the mRNA upon degradation of the polypeptide by a selected  
4 proteolytic agent, and the step of identifying the polypeptide encoded by the mRNA  
5 comprises subjecting polypeptides in the sample to degradation by the agent and  
6 identifying actual proteolytic fragments in the sample having masses that correspond to  
7 the masses of the predicted fragments.

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